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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,924	10/31/2000	Hiroyoshi Hidaka	198323US0PCT	6890

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EXAMINER	
TRAN, MY CHAU T	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,924	HIDAKA ET AL.	
	Examiner	Art Unit	
	MY-CHAU T. TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6,9-12 and 14-16* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6,9-12,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application and Claims Status

1. Applicant's amendment and response filed 09/13/05 is acknowledged and entered. Claim 5 has been amended.

2. The amendment filed on 02/09/2005: cancelled claims 7 and 8; amended claims 5, 9, and 10.

1. Claims 3, and 13 were canceled and Claims 5, and 14 were amended by the amendment filed on 3/01/2004.

2. Claims 2, and 4 are canceled, and claims 15-16 are added by the amendment filed on 6/30/2003.

3. Claim 1 is canceled, and claims 5-14 are added by the amendment filed on 5/08/2002.

4. Claims 5, 6, 9-12, and 14-16 are pending.

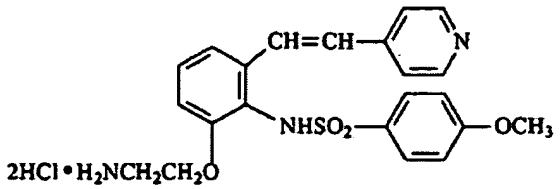
Election/Restrictions

5. Applicant has elected the following species for the elected invention (Claims 5-16):

   a. A species of antigenic substance is serum albumin.

   b. A species of chemical cross-linker is glutaraldehyde.

   c. A species of drug is drug A, which has the following structure:



6. Claim 14 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to ***a nonelected species***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed 8/30/02 and 10/9/02.

Priority

7. This application is a 371 of PCT/JP98/01712 filed 4/15/1998.

8. Claims 5, 6, 9-12, 15, and 16 are treated on the merit in this Office Action.

Maintained Rejection(s)

Claim Rejections - 35 USC § 103

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 5, 6, 9-10, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580), Odink et al. (US Patent 5,821,336, Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22.

Gram et al. disclose a method for *in vitro* detection of a gene encoding a drug-targeted protein (Abstract; pg. 3578, left col., line 19 to right col. line 4). The method comprises the phage displaying low affinity Fabs binding to a progesterone-bovine serum albumin conjugate (drug-serum albumin) were isolated from the library (pg. 3578, left col., line 19 to right col. line 4; pg. 3577, left col., lines 44-62). The drug-targeted protein comprise of progesterone-bovine serum albumin wherein the progesterone bind to the bovine serum albumin via a linker comprising 3-(*O*-carboxymethyl) oxime (pg. 3577, left col., lines 47-48). The phage display comprises *Escherichia coli* (pg. 3577, left col., lines 39-43) (refers to claims 6 and 15). The library comprises murine cDNA expression library (pg. 3577, left col., lines 1-34) (refers to claim 7). Additionally with regards to claims 8-10, the type of cDNA expression library would be a choice of experimental design and is considered within the purview of the cited prior art.

The method of Gram et al. differ from the presently claimed invention by failing to include the chemical cross-linker such as glutaraldehyde as the linker that couples the drug to the antigenic substance. However the instant specification on page 3 discloses that "*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance*" (see specification lines 19-22). Additionally, glutaraldehyde is a known bifunctional linkers use to couple drug to an antigenic substance as disclosed by Pecht et al. Pecht et al. disclose the method of forming a drug-BSA conjugate (col. 4, lines 13-26). The method comprises using glutaraldehyde as a bifunctional reagent to couple the drug to BSA (bovine serum albumin). Thus it would be obvious to one skilled in the art to use different type of bifunctional linkers to couple the drug to an antigenic substance since the instant specification on page 3 discloses that

"*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance*" (see specification lines 19-22).

The method of Gram et al. differs from the presently claimed invention by failing to include using cDNA expression library from human cell.

Odink et al. disclose the methods for producing human polypeptides using methods of recombinant DNA technology (see e.g. col. 1, line 66 to col. 2, line 28; col. 5, lines 32-46; col. 6, line 2 thru col. 8, line 62). One method comprises producing cDNA expression library from human placenta cell (see e.g. col. 8, lines 14-41).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include using cDNA expression library from human cell as taught by Odink et al. in the method of Gram et al. One of ordinary skill in the art would have been motivated to include using cDNA expression library from human cell in the method of Gram et al. for the advantage of providing polypeptides, especially human polypeptides, from the methods of recombinant DNA technology that can be use in screening for pharmaceutical compounds (Odink: col. 1, line 66 to col. 2, line 28) since both of Gram et al. and Odink et al. disclose the method of making cDNA from mRNA (Gram: pg. 3577, left col., lines 1-34; Odink: col. 8, lines 14-20). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Gram et al. and Odink et al. because Odink et al. disclose that cDNA from human cell are well known in the art (Odink: col. 7, line 57 thru col. 8, line 62).

11. Claims 11-12, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580), Odink et al. (US Patent 5,821,336, Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22 as applied to claims 5-10, and 15 above, and further in view of Barbas III et al. (*Proc. Natl. Acad. Sci. USA*, **1991**, 88:7978-7982).

Gram et al. disclose a method for *in vitro* detection of a gene encoding a drug-targeted protein (Abstract; pg. 3578, left col., line 19 to right col. line 4). The method comprises the phage displaying low affinity Fabs binding to a progesterone-bovine serum albumin conjugate (drug-serum albumin) were isolated from the library (pg. 3578, left col., line 19 to right col. line 4; pg. 3577, left col., lines 44-62). The phage display comprises *Escherichia coli* (pg. 3577, left col., lines 39-43) (refers to claims 6 and 15). The library comprises murine cDNA expression library (pg. 3577, left col., lines 1-34) (refers to claim 7). Additionally with regards to claims 8-10, the type of cDNA expression library would be a choice of experimental design and is considered within the purview of the cited prior art. Both Gram et al. and Pecht et al. disclose using a drug-BSA conjugate to bind to an antibody (Gram: pg. 3578, right col., lines 1-4; Pecht: col. 4, lines 49-68). Gram et al. disclose drug-targeted protein comprise of progesterone-bovine serum albumin, wherein the progesterone bind to the bovine serum albumin via a linker comprising 3-(*O*-carboxymethyl)oxime.

Furthermore, the method of Gram et al. differ from the presently claimed invention by failing to include the chemical cross-linker such as glutaraldehyde as the linker that couples the drug to the antigenic substance. However the instant specification on page 3 discloses that "*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group*

which cross-links a functional group of the drug and a functional group of the antigenic substance" (see specification lines 19-22). Additionally, glutaraldehyde is a known bifunctional linkers use to couple drug to an antigenic substance as disclosed by Pecht et al. Pecht et al. disclose the method of forming a drug-BSA conjugate (col. 4, lines 13-26). The method comprises using glutaraldehyde as a bifunctional reagent to couple the drug to BSA (bovine serum albumin). Thus it would be obvious to one skilled in the art to use different type of bifunctional linkers to couple the drug to an antigenic substance since the instant specification on page 3 discloses that "*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance*" (see specification lines 19-22).

The combination of Gram et al., Odink et al., and Pecht et al. is obvious over the presently claimed invention, but the combination differ from the presently claimed invention by failing to include employing a membrane to capture phage from plated phage culture.

Barbas III et al. disclose a method of colony screening of panned libraries (pg. 7979, right col., lines 12-27). The method comprises using nitrocellulose filters (membrane) with isopropyl 9-D-thiogalactopyranoside to capture the phage from plated phage culture (pg. 7979, right col., lines 12-16) (refers to claims 11-12, and 16).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include employing a membrane to capture phage from plated phage culture as taught by Barbas III et al. in the method of Gram et al. and Pecht et al. One of ordinary skill in the art would have been motivated to include employing a membrane to capture phage from plated phage culture in the method of Gram et al. and Pecht et al. because Gram et al.

incorporated the method of Barbas III et al. by reference into the disclosed colony screening method of panned libraries (Gram: pg. 3577, left col., lines 57-60). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Gram et al., Pecht et al., and Barbas III et al. because Gram et al. uses Barbas III et al. colony screening method of panned libraries (Gram: pg. 3577, left col., lines 57-60).

Withdrawn Rejection(s)

12. The rejections of claims 5, 6, 9-12, 15, and 16 under 35 USC 112, second paragraph, as being indefinite has been withdrawn in light of applicant's amendments of claim 5.

Response to Arguments

13. Applicant's argument directed to the rejection under 35 USC 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580), Odink et al. (US Patent 5,821,336, Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22 for claims 5, 6, 9-10, and 15 was considered but they are not persuasive for the following reasons.

Applicant argues that the combine teachings of Gram et al., Odink et al., Pecht et al., and the specification disclosure on page 3, lines 19-22 is not obvious over the instant claimed invention because 1) the teaching of Gram et al. and Pecht et al. are non-analogous art, and 2) there is no motivation to combine the teaching of Gram et al. and Odink et al. Thus, the combine teachings of Gram et al., Odink et al., Pecht et al., and the specification disclosure on page 3, lines 19-22 is not obvious over the instant claimed invention.

Applicant's arguments are not convincing since the combine teachings of Gram et al., Odink et al., Pecht et al., and the specification disclosure on page 3, lines 19-22 do render the method of the instant claims *prima facie* obvious.

First, in response to applicant's argument that the teaching of Gram et al. and Pecht et al. is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, both Gram et al. and Pecht et al. disclose using a drug-BSA conjugate to bind to an antibody, i.e. analogous art, (Gram: pg. 3578, right col., lines 1-4; Pecht: col. 4, lines 49-68). Additionally, the instant specification on page 3 discloses that '*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance*' (lines 19-22). Thus it would be obvious to one skilled in the art to use different type of bifunctional linkers to couple the drug to an antigenic substance such that it would be a choice of experimental design.

Second, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine the teaching of Gram et al. and Odink et al. is

found in the teaching of Odink et al., i.e. the advantage of providing polypeptides, especially human polypeptides, from the methods of recombinant DNA technology that can be use in screening for pharmaceutical compounds (Odink: col. 1, line 66 to col. 2, line 28). Furthermore, both of Gram et al. and Odink et al. disclose the method of making cDNA from mRNA, i.e. analogous art (Gram: pg. 3577, left col., lines 1-34; Odink: col. 7, line 57 thru col. 8, line 20).

Third, in response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

Therefore, the combine teachings of Gram et al., Odink et al., Pecht et al., and the specification disclosure on page 3, lines 19-22 do render the method of the instant claims *prima facie* obvious, and the rejection is maintained.

14. Applicant's argument directed to the rejection under 35 USC 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580), Odink et al. (US Patent 5,821,336, Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22 as applied to claims 5-10, and 15 above, and further in view of Barbas III et al. (*Proc. Natl. Acad. Sci. USA*, **1991**, 88:7978-7982) for claims 11-12, and 16 was considered but they are not persuasive for the following reasons.

Applicant alleges that the combine teachings of Gram et al., Odink et al., Pecht et al., the specification disclosure on page 3, lines 19-22, and Barbas III et al. is not obvious over the instant claimed invention because 1) the teaching of Gram et al. and Pecht et al. are non-

analogous art, and 2) there is no motivation to combine the teaching of Gram et al. and Odink et al. Thus, the combine teachings of Gram et al., Odink et al., Pecht et al., and the specification disclosure on page 3, lines 19-22 is not obvious over the instant claimed invention.

Applicant's arguments are not convincing since the combine teachings of Gram et al., Odink et al., Pecht et al., the specification disclosure on page 3, lines 19-22, and Barbas III et al. do render the method of the instant claims *prima facie* obvious.

First, in response to applicant's argument that the teaching of Gram et al. and Pecht et al. is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, both Gram et al. and Pecht et al. disclose using a drug-BSA conjugate to bind to an antibody, i.e. analogous art, (Gram: pg. 3578, right col., lines 1-4; Pecht: col. 4, lines 49-68). Additionally, the instant specification on page 3 discloses that '*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance*' (lines 19-22). Thus it would be obvious to one skilled in the art to use different type of bifunctional linkers to couple the drug to an antigenic substance such that it would be a choice of experimental design.

Second, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the

knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine the teaching of Gram et al. and Odink et al. is found in the teaching of Odink et al., i.e. the advantage of providing polypeptides, especially human polypeptides, from the methods of recombinant DNA technology that can be use in screening for pharmaceutical compounds (Odink: col. 1, line 66 to col. 2, line 28). Furthermore, both of Gram et al. and Odink et al. disclose the method of making cDNA from mRNA, i.e. analogous art (Gram: pg. 3577, left col., lines 1-34; Odink: col. 7, line 57 thru col. 8, line 20).

Third, in response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

Therefore, the combine teachings of teachings of Gram et al., Odink et al., Pecht et al., the specification disclosure on page 3, lines 19-22, and Barbas III et al. do render the method of the instant claims *prima facie* obvious, and the rejection is maintained.

Conclusion

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
November 28, 2005

PADMASHRI PONNALURI
PRIMARY EXAMINER